Remarks

I. Status of the Claims

At the time that the Office Action of January 23, 2009 was mailed, the claims pending in the present application were 38, 41-49, 52, 55, 56 and 58-64. No claims have been added or cancelled herein.

II. The Amendments

Claims 38 and 55 were amended to clarify that it is prior to modification that bacteria have a *yjgF* open reading frame with the nucleotide sequence of SEQ ID NO:1 and which encodes the polypeptide of SEQ ID NO:2. These amendments were made in response to the suggestion of the Examiner appearing in the first six lines on page 3 of the Office Action. In addition, the claims now require inactivation of *yjgF*.

Claim 58 was amended by adding a period at its end.

The amendments do not add new matter to the application and their entry is respectfully requested.

The Rejections

I. Rejection of Claims Under 35 USC §112, Second Paragraph

On pages 2-3 of the Office Action, claims 38, 41-47, 55-56 and 58-61 are rejected under 35 USC § 112, second paragraph, based upon the allegation that they require both modified and unmodified *yjgF* open reading frames. The Examiner suggests amending claims to indicate that the open reading frame has the sequence of SEQ ID NO:1 and encodes SEQ ID NO:2 *prior to modification.*

In response, Applicant has adopted the amendments suggested by the Examiner. It is therefore respectfully submitted that the present rejection has been overcome.

II. Rejection of Claims Under 35 USC §112, First Paragraph

A. Written Description

On pages 3-6 of the Office Action, claims are rejected based upon the written description requirement of 35 USC § 112, first paragraph. The Examiner argues that Applicant's claims encompass processes for producing L-threonine using bacteria of the genus Escherichia in which the *yjgF* open reading frame is attenuated. However, the only embodiment actually reduced to practice used *E. coli* and this is, allegedly, insufficient for one of skill in the art to recognize that disruptions in *yjgF* would produce a similar result in other bacteria.

Applicant respectfully traverses this rejection.

The written description requirement does not require that every embodiment within a claimed genus be in actual physical possession of the inventors. MPEP § 2163 states:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Enzo Biochem*, 323 F.3d at 964, 63 USPQ2d at 1613. For example, the presence of a restriction enzyme map of a gene may be relevant to a statement that the gene has been isolated. One skilled in the art may be able to determine whether the gene disclosed is the same as or different from a gene isolated by another by comparing the restriction enzyme maps. In contrast, evidence that the gene could be digested with a nuclease would not normally represent a relevant characteristic since any gene would be digested with a nuclease. Similarly, isolation of an mRNA and its expression to produce the protein of interest is strong evidence of possession of an mRNA for the protein.
>
> For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. >As explained by the Federal Circuit, "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met . even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must

> contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 USPQ2d 1001, 1007 (Fed. Cir. 2006).

Whether a reduction to practice of a single species is sufficient to meet the written description requirement for a claimed genus depends upon the extent to which the species is representative of other members of the genus. Thus, MPEP § 2163 states:

> A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004) . . .

Applicant's claims are limited to processes for producing L-threonine using bacteria with a *yjgF* open reading frame that has been functionally inactivated. They do not include all bacteria within the Escherichia genus but only those whose *yjgF* gene has the sequence of SEQ ID NO:1. Thus, the claims are limited to a group of bacteria that should be similar to the species reduced to practice and require the disruption of the same gene sequence. Applicant believes that, given these limitations, one of ordinary skill in the art could predict the operability of all of the embodiments claimed, *i.e.*, it is reasonable to expect that other bacteria of the Escherichia genus that express the same *yjgF* gene and that have had this gene inactivated will behave similarly with respect to the production of L-threonine. Applicant cannot see anything in the Examiner's arguments that would lead to a different conclusion. Therefore, under the criteria set forth in MPEP § 2163, it is submitted that the written description requirement for the presently pending claims has been met.

B. Enablement

On pages 6-9 of the Office Action, claims 38, 41-47, 55-56 and 58-61 are rejected based upon the enablement requirement of 35 USC § 112, first paragraph. The Examiner argues that, although claims are enabled for embodiments in which modifications result in the inactivation of the *yjgF* open reading frame, other modifications are not enabled.

In response, Applicant has limited claims to bacteria in which *yjgF* is inactivated. It is therefore respectfully submitted that the Examiner's rejection has been overcome.

III. Rejection of Claims Under 35 USC § 103

On pages 10-14 of the Office Action, the Examiner repeats a rejection of claims based upon the allegation that they are obvious in light of the combination of Volz (*Prot. Sci. 8*:24-28 (1999)); Enos-Berlage (*J. Bacteriol. 180*:6519-6528 (1998)), Verkhovskaya, *et al.*, (*Microbiol. 147*:3005-3013 (2001)) and Promega Technical Bulletin No. 117 (September 2002)). These references have all been discussed in previous responses and therefore Applicant will try to focus on arguments that are either newly raised in the present Office Action or that the Examiner seems to be primarily relying upon.

On page 10 of the Office Action, the Examiner seems to agree that the objective of the combination of references is not the isolation of amino acids but argues that despite this, one practicing the combined method would perform each of the steps in the claimed process. This is essentially the inherency argument that the Examiner made previously, *i.e.*, an argument that if one combined all of the processes taught by the references, a method would result in which Applicant's process occurred even though those practicing the process are unaware of it. As discussed in previous responses, it is Applicant's position that there is no legal basis for a rejection of this type. The references do not suggest inactivating the *yjgF* gene in bacteria in order to increase threonine production and then using these bacteria to fermentatively produce the amino acid. In the absence of such a suggestion, prima facie obviousness cannot be established.

On page 11, the Examiner argues that the cell free lysate disclosed in Enos-Berlage represents the isolation of threonine as a product. Applicant is not entirely sure of the portion of Enos-Berlage that the Examiner is referring to. If it is the cloning of the *yjgF* gene (page 6520, right side), then the end product of the isolation appears to be DNA not L-threonine. Enos-Berlage never teaches using bacteria with inactivated *yjgF* genes to fermentatively make threonine. The most relevant teaching concerns isoleucine and, in this regard, the reference does not teach increased production. Applicant submits that construing Enos-Berlage as teaching a method for fermentatively making threonine is an attempt to read in elements of Applicant's claims, rather than a fair reading of what the reference plainly says.

On page 12 of the Office Action, the Examiner argues that, based upon the way that the word "isolated" is used in the application, it has been defined to include preparations of L-threonine that have been obtained without any purification at all. The particular phrase that the Examiner points to reads: "the desired L-amino acid is isolated, constituents of the fermentation broth and/or the biomass in its entirety or portions thereof (>0 to 100%) thereof optionally remaining in the product."

In response, Applicant submits that the sections of the application referred to by the Examiner do not define term "isolated" but merely use the term as part of a phrase that appears to try to cover both purified and unpurified products. It is admittedly awkward, and potentially confusing, terminology. However, it is no longer part of the claims that are pending in the application. If the Examiner believes that further clarification would be helpful, Applicant would be agreeable to amending claims to refer to "purifying L-threonine" in claims 38 and 48. The specific word "purifying" does not appear in the application but this concept is clearly present.

Finally, on page 13 of the Office Action, the Examiner repeats the assertion that if the cited references were combined, the claimed method would inherently be present. Again, Applicant believes that this is an improper mixing of standards used for obviousness and standards used for novelty. Applicant knows of no basis for combining references to arrive at an invention different from one that is claimed (in this case, a process other than a method for fermentatively producing L-threonine) and then rejecting claims based upon the claimed method being inherently present.

Conclusion

In light of the discussion above, Applicant believes that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims now pending in the application be allowed. Early notice to this effect is earnestly solicited.

If, in the opinion of the Examiner, a phone may expedite the prosecution of this application, the Examiner is invited to call Applicant's undersigned attorney at (240) 683-6165.

Respectfully submitted,
LAW OFFICE OF MICHAEL A. SANZO, LLC

By: /Michael A. Sanzo/
Michael A. Sanzo
Reg. No. 36,912
Attorney for Applicant

Date: April 25, 2009
15400 Calhoun Drive, Suite 125
Rockville, Md. 20855
(240) 683-6165